LISTING OF THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

1. (Previously presented) A recombinant protein variant with the ability to induce a protective immune response to a naturally occurring allergen,

wherein the protein variant is a variant of a scaffold protein, said scaffold protein has a three-dimensional folding pattern that is structurally similar to that of the naturally occurring allergen, compared to the scaffold protein, comprises two or more primary mutations spaced by at least one non-mutated amino acid residue, each primary mutation introducing into the scaffold protein at least one amino acid residue identical or homologous to the amino acid residue or residues in corresponding position in the naturally occurring allergen,

and the recombinant protein variant has, compared to the scaffold protein, an increased affinity and/or binding capacity to IgE antibodies that are specific to the naturally occurring allergen.

2. (Original) A protein variant according to claim 1, wherein the protein variant has a reduced ability to induce histamine release compared to the naturally occurring allergen.

3. (Previously presented) A protein variant according to claim 2 wherein the ability to induce histamine release is reduced 2 - 10,000 fold.

4. (Original) A protein variant according to claim 1, which further comprises one or more secondary mutations introducing into the scaffold protein amino acid residues, which are not present in the corresponding position in the naturally occurring allergen.

5. (Previously presented) A protein variant according to claim 1 comprising 2 to 50 primary mutations.

6. (Previously presented) A protein variant according to claim 1, wherein the scaffold protein has a level of amino acid identity with the naturally occurring allergen of between 20 and 60 %.

7. (Original) A protein variant according to claim 1, wherein the protein variant compared to the naturally occurring allergen has a decreased binding capacity with respect to antibodies specific to the naturally occurring allergen.

8. (Previously presented) A protein variant according to claim 1, wherein the said binding capacity is increased to at least 10%, of the antibody binding capacity of the natural allergen.

9. (Original) A protein variant according to claim 1, wherein at least one of the primary mutations is a substitution.

10. (Original) A protein variant according to claim 1, wherein the introduction of at least one of the primary mutations is a deletion and/or an addition.

11. (Previously presented) A protein variant according to claim 1, wherein the deconvoluted CD-spectra of the protein variant deviates less than 30% compared to the deconvoluted CD-spectra of the naturally occurring allergen.

12. (Original) A protein variant according to claim 1, wherein all primary mutations are located within a surface region having an area of about 600-900 $Å^2$.

13. (Original) A protein variant according to claim 1, wherein the primary mutations comprise mutation of surface-exposed amino acids.

14. (Previously presented) A protein variant according to claim 13, wherein the primary amino acid residues to be mutated have a solvent accessibility of above 20 %.

15. (Original) A protein variant according to claim 1, wherein one or more of the mutations are carried out by site-directed mutagenesis.

16. (Original) A protein variant according to claim 1, wherein one or more of the mutations are carried out by DNA shuffling.

17. (Original) A protein variant according to claim 1 obtained by gene library methods.

18. (Canceled)

19. (Previously presented) A protein variant with the ability to induce a protective immune response to a naturally occurring allergen, obtainable by a method comprising the steps of:

- selecting a scaffold protein, said scaffold protein having a three-dimensional folding pattern that is structurally similar to that of the naturally occurring allergen,
- introducing two or more primary mutations, that are spaced by at least one non-mutated amino acid residue, into the scaffold protein, each primary mutation introducing into the scaffold protein at least one amino acid residue identical or homologous to the corresponding amino acid residue or residues in the naturally occurring allergen, and
- the protein variant having, compared to the scaffold protein, an increased affinity and/or binding capacity to IgE antibodies that are specific to the naturally occurring protein.

20. (Original) A protein variant according to claim 1, wherein the naturally occurring allergen is an inhalation allergen.

21. (Original) A protein variant according to claim 20, wherein the naturally occurring allergen is a pollen allergen.

22. (Original) A protein variant according to claim 21, wherein the naturally occurring allergen is a pollen allergen originating from the taxonomic order of *Fagales*, *Oleales* or *Pinales*.

23. (Original) A protein variant according to claim 22, wherein the naturally occurring allergen is *Bet v* 1.

24. (Original) A protein variant according to claim 23, wherein the scaffold protein is *Mal d* 1.

25. (Previously presented) A protein variant according to claim 24, wherein the *Mal d* 1 scaffold is *Mal d* 1 2620 having Accession No. AJ488060 and wherein at least two primary mutations are selected from the group consisting of: (E12V, E12I, E12M, E12L), P16A, (H40S, H40T), I43N, L44I, D47N, G65K, K70R, (E76H, E76R, E76K, E76Q), S107T, G108P, +109D, S110G, E129A, K152L, (P154S, P154T), P155S and optionally one or more secondary mutations are selected from the group consisting of: N28X, preferably N28T, K32X, preferably K32Q, E45S, E96X, +159X.

26. (Previously presented) A protein variant (rMal d 1 (2781)) according to claim 24 comprising the sequence defined in SEQ ID NO 2.

27. (Previously presented) A protein variant (rMal d 1 (2762)) according to claim 24 comprising the sequence as defined in SEQ ID NO 3.

28. (Previously presented) A protein variant according to claim 24 wherein the *Mal d* 1 scaffold is *Mal d* 1 2620 having Accession No. AJ488060 and wherein the variant comprises at least two primary mutations selected from the group consisting of: (E12V, E12I, E12M, E12L), (H40S, H40T), (E76H, E76R, E76K), E129A, (P154S, P154T), and optionally one or more secondary mutations selected from the group consisting of: E8X, N28X, K32X, E96X, +159X.

29. (Original) A protein variant according to claim 23 wherein the scaffold protein of Bet v 1 is Dau c 1.

30. (Previously presented) A protein variant according to claim 29, wherein the Dau c 1 scaffold protein is Accession No. T14325 and wherein at least two primary mutations are selected from the group consisting of: (S12V, S12L, S12I, S12M), S14P, E16A, P105A, A107P, (A148S, A148T), (I151L, I151V, I151M), (N153H, N153K, N153R), (+154S, +154T), (+155D, +155E), +156A, (+157Y, +157F), (+158N, +158Q), (K39S, K39T), (K44E, K44D), (V52I, V52M, V52L), (I54K, I54R, I54H), (T64K, T64R, T64H),

(T65Y, T65F, T65W), (T67K, T67R, T67H), D86E, L91G, (G92D, G92E) and optionally one or more secondary mutations are selected from the group consisting of: K32X, E42X, E59X, R69X, E95X, K122X, E8X, T10X, D25X, D46X, D108X.

31. (Previously presented) A protein variant according to claim 29 wherein the Dau c 1 scaffold protein is Accession No. T14325 and comprises at least two primary mutations selected from the group consisting of: (S12V, S12L, S12I, S12M), S14P, E16A, P105A, A107P, (A148S, A148T), (I151L, I151V, I151M), (N153H, N153K, N153R), (+154S, +154T), (+155D, +155E), +156A, (+157Y, +157F), (+158N, +158Q) and optionally one or more secondary mutations selected from the groups consisting of: K32X, E42X, E59X, R69X, E95X, K122X.

32. (Previously presented) A protein variant according to claim 29 wherein the Dau c 1 scaffold protein is Accession No. T14325 and comprises at least two primary mutations selected from the group consisting of: (K39S, K39T), (K44E, K44D), (V52I, V52M, V52L), (I54K, I54R, I54H), (T64K, T64R, T64H), (T65Y, T65F, T65W), (T67K, T67R, T67H), D86E, L91G, (G92D, G92E) and optionally at least one secondary mutation is selected from the group consisting of: E8X, T10X, D25X, K32X, D46X, E59X, E95X, D108X, K122X.

33-51. (Canceled)

52. (Previously presented) A recombinant protein variant with the ability to modulate an immune response to a naturally occurring allergen, wherein

- the naturally occurring allergen is selected from the group consisting of plant, grass, food, and mite allergens,

- the protein variant is a variant of a scaffold protein, said scaffold protein has a three-dimensional folding pattern that is similar to that of a naturally occurring allergen, the protein variant compared to the scaffold protein comprises at least two or more primary mutations spaced by at least one non-mutated amino acid residue, each primary mutation introducing into the scaffold protein at least one

amino acid residue identical or homologous to at least one amino acid residue present in the corresponding position in the natural occurring allergen, and

- the protein variant has, compared to the scaffold protein, an increased affinity and/or binding capacity to IgE antibodies that are specific to the naturally occurring protein.

53. (Previously presented) A recombinant protein variant with the ability to modulate an immune response to a naturally occurring allergen, wherein

- the protein variant is a variant of a scaffold protein, said scaffold protein has a three-dimensional folding pattern that is similar to that of the naturally occurring allergen,

- the scaffold protein having a level of sequence identity with the naturally occurring allergen of between 30 and 50 %,

- the protein variant compared to the scaffold protein comprises at least two or more primary mutations spaced by at least one non-mutated amino acid residue, each primary mutation introducing into the scaffold protein at least one amino acid residue identical or homologous to at least one amino acid residue present in the corresponding position in the natural occurring allergen, and

- the protein variant has, compared to the scaffold protein, an increased affinity and/or binding capacity to IgE antibodies that are specific to the naturally occurring.

54. (Previously presented) A recombinant protein variant with the ability to modulate an immune response to a naturally occurring allergen, wherein

- the protein variant is a variant of a scaffold protein, said scaffold protein has a three-dimensional folding pattern that is similar to that of a naturally occurring allergen,

- the deconvoluted CD-spectra of the protein variant deviates less than 30% compared to the deconvoluted CD-spectra of the naturally occurring allergen,

- the protein variant compared to the scaffold protein comprises at least two or more primary mutations spaced by at least one non-mutated amino acid residue, each primary mutation introducing into the scaffold protein at least one amino acid residue identical or homologous to at least one amino acid residue present in the corresponding position in the natural occurring allergen, and

- the protein variant has, compared to the scaffold protein, an increased affinity and/or binding capacity to IgE antibodies that are specific to the naturally occurring protein.

55. (Original) A pharmaceutical composition comprising protein variant according to any one of claims 1, 19 or 52-54 and a pharmaceutically acceptable carrier, excipient, or adjuvant.

56. (Original) A composition according to claim 55 comprising two or more recombinant protein variants, wherein each variant is defined by having at least one primary mutation, which is absent in at least one of the other variants.

57. (Previously presented) A composition according to claim 56 comprising 2 to 12 different protein variants.

58. (Canceled)

59. (Original) The pharmaceutical composition of claim 55 in the form of a vaccine against allergic reactions elicited by a naturally occurring allergen in patients suffering from allergy.

60-72. (Canceled)

73. (Original) A recombinant protein variant according to any one of claims 1, 19 or 52-54 comprising at least one T-cell epitope capable of stimulating a T-cell clone or T-cell line specific for the naturally occurring allergen.

74-75. (Canceled)

76. (Previously presented) A protein variant according to claim 5 comprising 2 to 40 primary mutations.

77. (Previously presented) A protein variant according to claim 5 comprising 3 to 25 primary mutations.

78. (Previously presented) A protein variant according to claim 5 comprising 4 to 15 primary mutations.

79. (Previously presented) A protein variant according to claim 5 comprising 5 to 12 primary mutations.

80. (Previously presented) A protein variant according to claim 6, wherein the scaffold protein has a level of amino acid identity with the naturally occurring allergen of between 30 and 50 %.

81. (Previously presented) A protein variant according to claim 8, wherein the said binding capacity is increased to at least 50% of the antibody binding capacity of the natural allergen.

82. (Previously presented) A protein variant according to claim 8, wherein the said binding capacity is increased to at least 100% of the antibody binding capacity of the natural allergen.

83. (Previously presented) A protein variant according to claim 11, wherein the deconvoluted CD-spectra of the protein variant deviates less than 20% compared to the deconvoluted CD-spectra of the naturally occurring allergen.

84. (Previously presented) A protein variant according to claim 11, wherein the deconvoluted CD-spectra of the protein variant deviates less than 10% compared to the deconvoluted CD-spectra of the naturally occurring allergen.

85. (Previously presented) A protein variant according to claim 14, wherein the primary amino acid residues to be mutated have a solvent accessibility of above 30 %.

86. (Previously presented) A protein variant according to claim 14, wherein the primary amino acid residues to be mutated have a solvent accessibility of above 40 %.

87. (Previously presented) A protein variant according to claim 14, wherein the primary amino acid residues to be mutated have a solvent accessibility of above 50 %.

88. (Previously presented) A recombinant protein variant according to claim 54, wherein the deconvoluted CD-spectra of the protein deviates less than 20% compared to the deconvoluted CD-spectra of the naturally occurring allergen.

89. (Previously presented) A recombinant protein variant according to claim 54, wherein the deconvoluted CD-spectra of the protein deviates less than 10% compared to the deconvoluted CD-spectra of the naturally occurring allergen.

90. (Previously presented) A composition according to claim 57 comprising 3 to 10 different protein variants.

91. (Previously presented) A composition according to claim 57 comprising 4 to 8 different protein variants.

92. (Previously presented) A composition according to claim 57 comprising 5 to 7 different protein variants.